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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/618,129	07/17/2000	Xiao Bing Wang	TRIM1	8510

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EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/618,129	WANG, XIAO BING	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,8,9,11-36 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,8,9,11-36 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/11/04 & 6/14/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 31, 2004 has been entered.

Status of the Application

2. Currently, claims 2-3, 8-9, 11-36 and 42 are pending and are rejected herein.

Information Disclosure Statement

3. The information disclosure statements filed on May 24, 2004 and June 9, 2004 comply with CFR 1.97, 1.98, and M.P.E.P. 609, and have been considered (see enclosed signed PTO-1449s).

Specification

4. The disclosure is objected to because:

A) It appears as if there is a typographical error on page 13. Page 13 recites:

> For example, if it is desired that the primer extension reaction be stopped opposite a "C" on the template strand, the non-terminating bases A, T and *G should be included in the primer extension reaction mixture, but not "G"*, which is the complement of "C". Thus, the absence of the complementary base will cause termination of the primer extension reaction with a similar result as adding a dideoxy terminator nucleotide, for example.

B) Claim 42 recites the third step as being (d), which should be amended to recite (c).

Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 2-9, 11-15, 17, 23-36 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Fahy et al. (WO 96/30545, previously cited).

Regarding Claims 2-3 and 42, Fahy teaches a method for detecting variations of a nucleotide at a defined site of a nucleic acid comprising:

(a) identifying a first form of a nucleic acid having a first nucleotide X at the defined site, wherein X is A, T, G, C, or U;

(b) performing a primer extension reaction on a nucleic acid sample containing a second nucleotide Y at the defined site using a primer extension reaction mixture comprising;

(i) a primer that hybridizes upstream of the defined site of the nucleic acid sample so that the first unpaired base immediately downstream of the 3' end of the primer is Y,

(ii) a nucleotide combination in which nucleotides complementary to X are omitted, the nucleotide mixture combination consisting of:

(1) dTTP or dUTP, dCTP, and dGTP when X is T and at least one of dTTP, dCTP, dGTP or dUTP is labeled with a detectable label, or

(2) dCTP, dGTP and dATP when X is A or U and at least one of dCTP,

dGTP and dATP is labeled with a detectable label, or

(3) dGTP, dATP, and dTTP or dUTP when X is G and at least one of dGTP, dATP, and dTTP or dUTP is labeled with a detectable label, or

(4) dATP, dTTP or dUTP, and dCTP when X is C and at least one of dATP, dTTP or dUTP, and dCTP is labeled with a detectable label; and

(c) analyzing the primer extension products formed in (b), wherein the presence of a labeled primer extension product indicates that Y does not equal X.

(See page 7, lines 18-37, page 8, especially page 8, lines 4-6, pages 13-16, especially page 16, lines 17-26, page 17, lines 1-3, pages 18-21, especially page 18, lines 11-14 and page 21, lines 27-31, pages 60-62, for example.)

Regarding Claim 8, Fahy teaches the labeled dNTPs (non-terminator nucleotides) are labeled with the same or different detectable markers (See pages 15-16 and page 21, lines 15-23 and 27-32, for example).

Regarding Claim 9, Fahy teaches the use of this invention with various labels such as radioactive or fluorescent labels (See pages 15-16 and page 21, lines 15-23, for example).

Regarding Claims 11-14, Fahy teaches that the primer extension reaction can be performed by enzymatic means using template dependent enzymes (i.e., T7 DNA polymerase, Klenow fragment, reverse transcriptase, etc.) (See pages 19-20, for example).

Regarding claims 15 and 17, Fahy teaches that the primer may contain biotin (See page 21, lines 15-26, for example).

Regarding Claims 23-36, Fahy teaches the source of the target nucleic acid of interest can be any form of RNA or DNA , obtained via amplification (for example), from any source such as

from a human, animal, or microbe, and can comprise non-natural nucleotide analogs (See pages 9, 13-15, 17 and 58, for example).

Applicant's Argument

Applicant argues Fahy does not teach the recited nucleotide combinations. See page 10 of Applicant's response.

Response to Applicant's Argument

Applicant's argument has been considered, but is not persuasive for the following reasons. First, Fahy teaches the claimed method wherein, "synthesis of the extension products is accomplished by polymerase extension of the primers until a template nucleotide is read *or omitted which terminates synthesis*. For example a nucleotide in the template can be read for which *no complementary dNTP is available in the extension mixture, resulting in chain termination*." See page 19, lines 11-14. Furthermore, Fahy teaches dNTPs comprise dATP, dCTP, dGTP and dTTP (page 15, lines 10-16, Fahy also teaches the nucleic of interest can be RNA, which would result in the use of a dUTP). Accordingly, because Fahy teaches the dNTPs that satisfy the nucleotide combinations, and based on established, limited nucleic base pairing principles (e.g., A-T, C-G), Fahy inherently teaches the claimed nucleotide combinations.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 16 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fahy et al. (WO 96/30545, previously cited), as applied to claims 2-9, 11-15, 17, 23-37 and 39-41 above, and further in view of Soderlund (US 6,013,431).

The teachings of Fahy are presented above. Specifically, Fahy teaches the method of detection using a primer labeled with biotin. Fahy does not teach the primer permits affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest or that a solid support may be used in the separation process.

However, Soderlund teaches a detection method wherein the primer may contain an attachment moiety (i.e., biotin, antigens, etc.) (See col. 6, ln. 16-31, for example), that permits affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest (col. 6, ln. 53 to col. 7, ln. 26, for example), and furthermore, that a solid support may be used in the separation process (col. 6-7, for example). Soderlund teaches using attachment moieties (which can be used for linkage to a solid support) is advantageous in aiding the detection process by determining which strand the variable nucleotide occurs (col. 6, lines 7-9), purifying the reaction to ensure only bound material is analyzed (col. 6, lines 55-63), and making

it possible to reuse the target nucleic acid if multiple determinations are to be performed on the same target sequence of interest (col. 6, lines 63-67).

Accordingly, in view of the teachings of Soderlund, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Fahy so as to have used a primer comprising an attachment moiety which permits affinity separation of the primer from the unincorporated reagent and/or the nucleic acid of interest and to have used a solid support in the separation process. One of ordinary skill in the art would have been motivated to modify the method of Fahy in order to have achieved the benefit of aiding the detection process by determining which strand the variable nucleotide occurs, purifying the reaction to ensure only bound material is analyzed, and making it possible to reuse the target nucleic acid if multiple determinations are to be performed on the same target sequence of interest.

Conclusion

10. No claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Alexander H. Spiegler
November 12, 2004

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